

The American Psychiatric Association Practice Guideline for the Prevention and Treatment of Delirium

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In November 2024, the American Psychiatric Association (APA) Board of Trustees approved “*The American Psychiatric Association Practice Guideline for the Prevention and Treatment of Delirium*.” The full guideline is available at APA’s Practice Guidelines web page and describes aspects of guideline implementation that are relevant to individual patients’ circumstances and preferences.

The goal of this guideline is to prevent the development of delirium in at-risk individuals and to improve the quality of care and treatment outcomes for patients with delirium. Patients with delirium often experience a longer and more complicated hospital stay, difficulties in participating in their care, challenges in developing a safe discharge plan, and increased morbidity and mortality (Fong and Inouye 2022; Marcantonio 2017; Prendergast et al. 2022). With early recognition of delirium, potential causes can be identified and addressed, and clinical outcomes can be improved (Devlin et al. 2018). Despite these benefits, delirium is widely known to be underdetected, especially in the acute hospital setting (Bush et al. 2017; Carpenter et al. 2021; Geriatric Medicine Research Collaborative 2019). Research suggests that even highly trained health care professionals may be prone to overlooking delirium in the absence of validated screening tools, underscoring the value of routine assessment for ensuring safe and high-quality care (American College of Surgeons 2019; Bush et al. 2017; Devlin et al. 2007; Grossmann et al. 2014; Kotfis et al. 2018; Spronk et al. 2009). This practice guideline aims to help clinicians improve the detection of delirium and the care and well-being of their patients by reviewing current evidence and providing evidence-based statements (Box 1) that are intended to enhance knowledge and optimize the assessment and treatment of delirium.

The prevalence rates of delirium range widely depending on the patient population and treatment setting (e.g., age, hospital vs. outpatient setting, medical vs. cardiac unit, surgical vs. critical care unit). In emergency department settings,

delirium is present in up to one-third of patients, depending on age and referral source, but is often unrecognized (Chen et al. 2022; Lee et al. 2022; Oliveira J E Silva et al. 2021; O’Regan et al. 2018). A meta-analysis of 33 studies of adults (age 18 and older) on medical inpatient units reported an overall delirium occurrence rate of 23% (Gibb et al. 2020). The pooled prevalence of delirium among adults in intensive care units (ICUs) has been estimated at 31%, with a pooled incidence of 4%–11% depending on delirium motor subtype (Krewulak et al. 2018). In mechanically ventilated patients in ICUs, who are typically sedated and seriously ill, delirium appears to be extremely common, with an estimated prevalence of 75% (Mart et al. 2021). Delirium also occurs in ambulatory settings. For example, among older adult outpatients of a memory clinic in a psychiatric hospital (Quispel-Aggenbach et al. 2021), the rate of probable delirium was 19%.

Delirium exacts a significant economic toll on individuals, their families, and society because of factors such as lengthy hospital stays, ICU admissions, rehospitalizations, and lost wages from work absenteeism (Gou et al. 2021; Kinchin et al. 2021; Vasilevskis et al. 2018). For hospitalized inpatients, added costs due to delirium have been estimated at \$6.6–\$82.4 billion annually in the United States alone based on 2019 data (Kinchin et al. 2021). Direct 1-year health care costs of postoperative delirium specifically have been estimated at \$32.9 billion per year based on data from 2019 (Gou et al. 2021). Additionally, the 30-day incremental cumulative cost of delirium treated in the ICU is approximately \$18,000, or an additional \$600 per day (Vasilevskis et al. 2018). These costs are almost certainly an underestimate because of the significant mortality rates of patients with delirium in ICU settings (Vasilevskis et al. 2018).

Mortality and morbidity associated with delirium are both substantial in many patient populations. Delirium has been associated with increased mortality during general medical and critical care hospitalization (Hsieh et al. 2020) and



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more specifically with a 38% increase in the risk of death (Maldonado 2017). Postsurgical delirium has been reported to have a 30-day mortality rate of up to 10% compared with 1% in postsurgical patients without delirium (Jin et al. 2020). Delirium also increases the risk of death among patients with COVID-19, with a pooled mortality risk (44%) that is triple that of COVID-19 patients without delirium (Peterson et al. 2021).

Delirium has been linked to a host of deleterious outcomes and complications, including increased hospital and ICU lengths of stay, greater risk of rehospitalization, more time spent on mechanical ventilation, increased odds of cognitive dysfunction, greater frailty and risk of falls, persistent functional decline, greater likelihood of discharge to long-term-care facilities rather than to home, increased risk of respiratory and neurological sequelae, and higher odds of difficult and extended extubation (Fiest et al. 2021; Goldberg et al. 2020; Haley et al. 2019; Inouye et al. 2016; Kinchin et al. 2021; Maldonado 2017). Even after remission, patients can continue to experience protracted cognitive impairment, ongoing functional decline, a heightened mortality risk, subsequent rehospitalizations and emergency department visits, and an increased need for long-term care (Fiest et al. 2021; Goldberg et al. 2020; Inouye et al. 2016; Kukreja et al. 2015; Richardson et al. 2021; Salluh et al. 2015; Wolters et al. 2014).

Delirium can be a significant strain on patients and caregivers. Contributors include psychosocial distress, such as anxiety and fear, and the high costs and health care needs associated with co-occurring conditions (e.g., Alzheimer's dementia, other end-stage diseases) (Fong et al. 2019). Delirium-related distress in patients—which can include posttraumatic stress disorder (PTSD)-like symptoms, anxiety, and depression—appears associated with increased severity of the underlying critical illness, greater cognitive impairment, and longer duration of delirium (MacLulich et al. 2022; Williams et al. 2020). Furthermore, psychosocial consequences of distress during delirium, such as delirium recall or memories, can be upsetting to patients and may persist for months after the condition resolves (Williams et al. 2020).

For all these reasons, this practice guideline focuses on preventing the development of delirium in at-risk individuals and improving the quality of care for patients with delirium, thereby reducing the mortality, morbidity, and significant psychosocial and health consequences of this important psychiatric condition.

OVERVIEW OF THE DEVELOPMENT PROCESS

This guideline was developed using a clearly defined and transparent process that is intended to be consistent with the recommendations of the Institute of Medicine (2011) and the Principles for the Development of Specialty Society Clinical Guidelines of the Council of Medical Specialty

Societies (2017). Parameters used for the guideline's systematic review are included with the guideline appendices. The APA website features a full description of the guideline development process.

RATING THE STRENGTH OF RESEARCH EVIDENCE AND RECOMMENDATIONS

Development of guideline statements entails weighing the potential benefits and harms of the statement and then identifying the level of confidence in that determination. This concept of balancing benefits and harms to determine guideline recommendations and strength of recommendations is a hallmark of GRADE (Grading of Recommendations Assessment, Development and Evaluation), which is used by many professional organizations around the world to develop practice guideline recommendations (Guyatt et al. 2013). Our level of confidence in a guideline statement is informed by available evidence, which includes evidence from clinical trials (identified through systematic review) as well as expert opinion and patient values and preferences. In assessing available evidence, harms are broadly defined and may include serious adverse events, less serious adverse events that affect tolerability, minor adverse events, negative effects of the intervention on quality of life, barriers and inconveniences associated with treatment, direct and indirect costs of the intervention (including opportunity costs), and other negative aspects of the treatment that may influence decision making by the patient, the clinician, or both.

A detailed description of research evidence related to the effects of multicomponent nonpharmacological interventions and pharmacological treatments in individuals with delirium can be found in the appendices accompanying the full guideline. For each guideline statement, the authors of the guideline have rated and described the type and strength of the available evidence as well as the factors, including patient preferences, that were used in determining the balance of benefits and harms. Each final rating was determined as described in the section “Guideline Development Process.”

GUIDELINE SCOPE

This practice guideline focuses on evidence-based multicomponent nonpharmacological and pharmacological interventions to prevent or treat delirium in adults. In addition, it includes statements related to assessment and treatment planning, which are an integral part of patient-centered care. As such, the scope of this document is shaped by recent diagnostic criteria for delirium as defined by *DSM-5-TR* and by the available evidence (American Psychiatric Association 2022). Unless otherwise specified, when the term *delirium* is used in this practice guideline, it should

BOX 1. Guideline statements^a

Assessment and Treatment Planning

1. APA *recommends* (1C) that patients with delirium or who are at risk for delirium undergo regular structured assessments for the presence or persistence of delirium using valid and reliable measures.
2. APA *recommends* (1C) that a patient's baseline neurocognitive status be determined to permit accurate interpretation of delirium assessments.
3. APA *recommends* (1C) that patients with delirium or who are at risk for delirium undergo a detailed review of possible predisposing or contributing factors.
4. APA *recommends* (1C) that a detailed medication review be conducted in patients with delirium or who are at risk for delirium, especially those with preexisting cognitive impairment.
5. APA *recommends* (1C) that physical restraints not be used in patients with delirium, except in situations when injury to self or others is imminent and only:
 - After review of factors that can contribute to racial/ethnic and other biases in decisions about restraint;
 - With frequent monitoring; and
 - With repeated reassessment of the continued risks and benefits of restraint use as compared with less restrictive interventions.
6. APA *recommends* (1C) that patients with delirium have a documented, comprehensive, and person-centered treatment plan.
7. APA *recommends* (1C) that patients with delirium or who are at risk for delirium receive multicomponent nonpharmacological interventions to manage and prevent delirium.
8. APA *recommends* (1C) that medications, including antipsychotic agents, be used to address neuropsychiatric disturbances of delirium only when all of the following criteria are met:
 - Verbal and nonverbal de-escalation strategies have been ineffective;
 - Contributing factors have been assessed and, as far as possible, addressed; and
 - The disturbances cause the patient significant distress and/or present a risk of physical harm to the patient or others.
9. APA *recommends* (1C) that antipsychotic agents not be used to prevent delirium or hasten its resolution.
10. APA *recommends* (1C) that benzodiazepines not be used in patients with delirium or who are at risk for delirium, including those with preexisting cognitive impairment, unless there is a specific indication for their use.
11. APA *suggests* (2B) that dexmedetomidine be used rather than other sedating agents to prevent delirium in patients who are undergoing major surgery or receiving mechanical ventilation in a critical care setting.
12. APA *suggests* (2C) that when patients with delirium are sedated for mechanical ventilation in a critical care setting, dexmedetomidine be used rather than other sedating agents.
13. APA *suggests* (2C) that melatonin and ramelteon not be used to prevent or treat delirium.

Transitions of Care

14. APA *recommends* (1C) that in patients with delirium or who are at risk for delirium, a detailed medication review, medication reconciliation, and reassessment of the indications for medications, including psychotropic medications, be conducted at transitions of care within the hospital.
15. APA *recommends* (1C) that when patients with delirium are transferred to another setting of care, plans for follow-up include:
 - Continued assessments for persistence of delirium;
 - Detailed medication review, medication reconciliation, and reassessment of the indications for medications, including psychotropic medications;
 - Assessment of consequences of delirium (e.g., post-traumatic symptoms, cognitive impairment); and
 - Psychoeducation about delirium for patients and their care partners.

Nonpharmacological Interventions

7. APA *recommends* (1B) that patients with delirium or who are at risk for delirium receive multicomponent nonpharmacological interventions to manage and prevent delirium.

Pharmacological Interventions

8. APA *recommends* (1C) that medications, including antipsychotic agents, be used to address neuropsychiatric disturbances of delirium only when all of the following criteria are met:
 - Verbal and nonverbal de-escalation strategies have been ineffective;

^aA recommendation (denoted by the numeral 1 after the guideline statement) indicates confidence that the benefits of the intervention clearly outweigh the harms. A suggestion (denoted by the numeral 2 after the guideline statement) indicates greater uncertainty. Although the benefits of the statement are still viewed as outweighing the harms, the balance of benefits and harms is more difficult to judge, or either the benefits or the harms may be less clear. With a suggestion, patient values and preferences may be more variable, and this can influence the clinical decision that is ultimately made. Each guideline statement also has an associated rating for the strength of supporting research evidence. Three ratings are used: high, moderate, and low (denoted by the letters A, B, and C, respectively) and reflect the level of confidence that the evidence for a guideline statement reflects a true effect based on consistency of findings across studies, directness of the effect on a specific health outcome, precision of the estimate of effect, and risk of bias in available studies (Agency for Healthcare Research and Quality 2014; Balshem et al. 2011; Guyatt et al. 2006).

be understood in a generic sense. Our comments pertain to delirium due to any cause with the exception of delirium related to withdrawal from alcohol or sedative, hypnotic, or

anxiolytic medications, which represents a physiologically discrete condition. Although other physiologically discrete conditions are likely to present with delirium, this practice

guideline does not differentiate these conditions because the literature in support of physiological subtypes of delirium remains in its early stages (Bowman et al. 2024).

The document scope is also affected by a number of limitations of the evidence as obtained by a systematic review of the literature through July 9, 2021. For example, most studies that were identified in the systematic review for this guideline included patients older than 50 and generally older than 65. Research participants were predominantly male, but in many studies, the sample was nearly evenly divided. However, studies of much older adults (age 85 and older) tended to have a predominance of female participants. Most studies also enrolled predominantly White participants or did not specify the racial, ethnic, or cultural characteristics of the sample. Study populations were typically drawn from ICUs or other inpatient hospital settings (e.g., general medical unit, postsurgical unit, cardiac unit), although some studies focused specifically on populations in long-term-care facilities, such as nursing homes.

Although delirium can present as hypoactive, hyperactive, or with a mixed level of activity, studies typically did not describe whether patients had a motor subtype of delirium. Individuals with hypoactive delirium likely were identified less often and, thus, were less likely to be represented in the evidence base. Medication-related sedation also may resemble delirium in some patients. Furthermore, in contrast to *DSM-5* (American Psychiatric Association 2013), *DSM-5-TR* (American Psychiatric Association 2022) now notes that an inability to respond to verbal or physical stimulation should be classified as an arousal disorder such as coma or stupor, and not delirium. The degree of arousal and the motor subtype of delirium may also influence the effects of interventions; misclassification could therefore alter study conclusions.

Our systematic review did not include studies on delirium related to withdrawal from alcohol or sedative, hypnotic, or anxiolytic medications because this condition differs in etiology, assessment, and treatment from other types of delirium. Studies on risk factors for delirium were also outside the scope of our systematic review, although we conducted targeted searches on delirium risk factors, and this topic has been reviewed by others (Bramley et al. 2021; Ormseth et al. 2023; Zaal et al. 2015). We also did not examine the effect of potential moderators of interventions for delirium because these were not reported consistently or in relation to primary outcomes.

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